

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

DAVIS, P ter D.

Atty. Ref.:

620-179

Serial No.

10/018,826

Group:

Filed:

December 21, 2001

Examiner:

For:

CHIMERIC PROTEINS MEDIATING TARGETED

APOPTOSIS

April 22, 2002

Assistant Commissioner for Patents Washington, DC 20231

Sir:

STATEMENT

The attached paper and computer-readable copies of the Sequence Listing are the same. No new matter has been added.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By:

B. J. Sadoff Reg. No. 36,663

BJS:eaw

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SEQUENCE LISTING

<110> Davis, Peter D <120> Chimeric proteins mediating targeted apoptosis <130> 620-179 <140> US 10/018,826 <141> 2001-12-21 <150> PCT/GB00/02449 <151> 2000-06-26 <150> GB 9914650.8 <151> 1999-06-24 <160> 22 <170> PatentIn Ver. 2.1 <210> 1 <211> 84 <212> PRT <213> Homo sapiens <400> 1 Lys Tyr Ile Thr Thr Ile Ala Gly Val Met Thr Leu Ser Gln Val Lys 5 1 Gly Phe Val Arg Lys Asn Gly Val Asn Glu Ala Lys Ile Asp Glu Ile Lys Asn Asp Asn Val Gln Asp Thr Ala Glu Gln Lys Val Gln Leu Leu 40 Arg Asn Trp His Gln Leu His Gly Lys Lys Glu Ala Tyr Asp Thr Leu 50 Ile Lys Asp Leu Lys Lys Ala Asn Leu Cys Thr Leu Ala Glu Lys Ile 70 75 Gln Thr Ile Ile <210> 2 <211> 86 <212> PRT <213> Homo sapiens <400> 2

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Lys Glu Phe Val Arg Arg Leu Gly Leu Ser Asp His Glu Ile Asp Arg Leu Glu Leu Gln Asn Gly Arg Cys Leu Arg Glu Ala Gln Tyr Ser Met 35 Leu Ala Thr Trp Arg Arg Thr Pro Arg Arg Glu Ala Thr Leu Glu Leu Leu Gly Arg Val Leu Arg Asp Met Asp Leu Leu Gly Cys Leu Glu Asp Ile Glu Glu Ala Leu <210> 3 <211> 1468 <212> DNA <213> Artificial Sequence <220> <221> CDS <222> (116)..(1411) <220> <223> Description of Artificial Sequence: Nucleic acid construct encoding a chimeric protein containing the extracellular domain of CD44H and the transmembrane and cytoplasmic domains of human Fas <400> 3 ccagcetetg ccaggttegg teegecatee tegtecegte eteegeegge ecetgeeeeg 60 cgcccaggga tectecaget cetttegece gegeeeteeg ttegeteegg acace atg Met gac aag ttt tgg tgg cac gca gcc tgg gga ctc tgc ctc gtg ccg ctg 166 Asp Lys Phe Trp Trp His Ala Ala Trp Gly Leu Cys Leu Val Pro Leu 10 age etg geg eag ate gat ttg aat ata ace tge ege ttt gea ggt gta 214 Ser Leu Ala Gln Ile Asp Leu Asn Ile Thr Cys Arg Phe Ala Gly Val 25 20 262 ttc cac gtg gag aaa aat ggt cgc tac agc atc tct cgg acg gag gcc Phe His Val Glu Lys Asn Gly Arg Tyr Ser Ile Ser Arg Thr Glu Ala 40 35 gct gac ctc tgc aag gct ttc aat agc acc ttg ccc aca atg gcc cag Ala Asp Leu Cys Lys Ala Phe Asn Ser Thr Leu Pro Thr Met Ala Gln 50 atq qaq aaa qct ctg agc atc gga ttt gag acc tgc agg tat ggg ttc Met Glu Lys Ala Leu Ser Ile Gly Phe Glu Thr Cys Arg Tyr Gly Phe

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	aac Asn 100								454
	aca Thr								502
	gtc Val								550
	gtt Val								598
	aat Asn								646
	agc Ser 180								694
	tac Tyr								742
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	cct Pro 260								934
	ctt Leu								982
	cag Gln								1030

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Ala Ala Asp Leu Cys Lys Ala Phe Asn Ser Thr Leu Pro Thr Met Ala 50 55 60

Gln Met Glu Lys Ala Leu Ser Ile Gly Phe Glu Thr Cys Arg Tyr Gly
65 70 75 80

Phe Ile Glu Gly His Val Val Ile Pro Arg Ile His Pro Asn Ser Ile Cys Ala Ala Asn Asn Thr Gly Val Tyr Ile Leu Thr Tyr Asn Thr Ser Gln Tyr Asp Thr Tyr Cys Phe Asn Ala Ser Ala Pro Pro Glu Glu Asp Cys Thr Ser Val Thr Asp Leu Pro Asn Ala Phe Asp Gly Pro Ile Thr Ile Thr Ile Val Asn Arg Asp Gly Thr Arg Tyr Val Gln Lys Gly Glu Tyr Arg Thr Asn Pro Glu Asp Ile Tyr Pro Ser Asn Pro Thr Asp Asp Asp Val Ser Ser Gly Ser Ser Ser Glu Arg Ser Ser Thr Ser Gly Gly Tyr Ile Phe Tyr Thr Phe Ser Thr Val His Pro Ile Pro Asp Glu Asp Ser Pro Trp Ile Thr Asp Ser Thr Asp Arg Ile Pro Ala Thr Arg Asp Gln Asp Thr Phe His Pro Ser Gly Gly Ser His Thr Thr His Gly Ser Glu Ser Asp Gly His Ser His Gly Ser Gln Glu Gly Gly Ala Asn Thr Thr Ser Gly Pro Ile Arg Thr Pro Gln Ile Pro Glu Trp Leu Ile Ile Leu Cys Leu Leu Leu Pro Ile Pro Leu Ile Val Trp Val Lys Arg Lys Glu Val Gln Lys Thr Cys Arg Lys His Arg Lys Glu Asn Gln Gly Ser His Glu Ser Pro Thr Leu Asn Pro Glu Thr Val Ala Ile Asn Leu Ser Asp Val Asp Leu Ser Lys Tyr Ile Thr Thr Ile Ala Gly Val Met Thr Leu Ser Gln Val Lys Gly Phe Val Arg Lys Asn Gly Val Asn Glu Ala Lys Ile Asp Glu Ile Lys Asn Asp Asn Val Gln Asp Thr Ala Glu Gln Lys Val Gln Leu Leu Arg Asn Trp His Gln Leu His Gly Lys Lys Glu Ala Tyr Asp Thr Leu Ile Lys Asp Leu Lys Lys Ala Asn Leu Cys Thr Leu Ala Gly Lys Ile Gln Thr Ile Ile Leu Lys Asp Ile Thr Ser Asp Ser Glu Asn Ser Asn Phe Arg Asn Glu Ile Gln Ser Leu Val

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      the extracellular and transmembrane domains of CD44H
      and the cytoplasmic domain of human Fas
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                                                              Met
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gac aag ttt tgg tgg cac gca gcc tgg gga ctc tgc ctc gtg ccg ctg
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Asp Lys Phe Trp Trp His Ala Ala Trp Gly Leu Cys Leu Val Pro Leu
age etg geg eag ate gat ttg aat ata ace tge ege ttt gea ggt gta
                                                                   214
Ser Leu Ala Gln Ile Asp Leu Asn Ile Thr Cys Arg Phe Ala Gly Val
                             25
ttc cac gtg gag aaa aat ggt cgc tac agc atc tct cgg acg gag gcc
                                                                   262
Phe His Val Glu Lys Asn Gly Arg Tyr Ser Ile Ser Arg Thr Glu Ala
                                                                   310
get gac etc tgc aag get ttc aat agc acc ttg eec aca atg gee cag
Ala Asp Leu Cys Lys Ala Phe Asn Ser Thr Leu Pro Thr Met Ala Gln
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Met Glu Lys Ala Leu Ser Ile Gly Phe Glu Thr Cys Arg Tyr Gly Phe
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                 70
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Ile Glu Gly His Val Val Ile Pro Arg Ile His Pro Asn Ser Ile Cys
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                                                      95
             85
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Tyr Asp Thr Tyr Cys Phe Asn Ala Ser Ala Pro Pro Glu Glu Asp Cys
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ggg Gly 290	gtg Val	aag Lys	aga Arg	aag Lys	gaa Glu 295	gta Val	cag Gln	aaa Lys	aca Thr	tgc Cys 300	aga Arg	aag Lys	cac His	aga Arg	aag Lys 305	1030
gaa Glu	aac Asn	caa Gln	ggt Gly	tct Ser 310	cat His	gaa Glu	tct Ser	cca Pro	acc Thr 315	tta Leu	aat Asn	cct Pro	gaa Glu	aca Thr 320	gtg Val	1078
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cat go	ga aa ly Ly	g aaa s Lys	gaa Glu 390	gcg Ala	tat Tyr	gac Asp	aca Thr	ttg Leu 395	att Ile	aaa Lys	gat Asp	ctc Leu	aaa Lys 400	aaa Lys	1318
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gac a		r Ser													1414
agc to Ser Lo			agto	gaaaa	aac a	aacaa	aatto	ca gt	tete	gagta	a tat	gcaa	atta		1466
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gactctggcg (gccgggtcgt t	ggccggggg ag	cgcgggca ccggg	gegage aggeegegte 1	80
				ctg tgc gcg ctg 2 Leu Cys Ala Leu	31
				ca aaa tta aaa 2 er Lys Leu Lys 30	79
gat cct gaa Asp Pro Glu	ctg agt tta Leu Ser Leu 35	aaa ggc acc Lys Gly Thr	cag cac atc a Gln His Ile M 40	atg caa gca ggc 3 Met Gln Ala Gly 45	27
				eat aaa tgg tct 3 His Lys Trp Ser 60	75
				ngc ata act aaa 4 Ger Ile Thr Lys 75	23
				ct tta acc ttg 4 Thr Leu Thr Leu	71
				gc aaa tat cta 5 Cys Lys Tyr Leu 110	19
				ca atc tat ata 5 Na Ile Tyr Ile 125	67
ttt att agt Phe Ile Ser	gat aca ggt Asp Thr Gly 130	aga cct ttc Arg Pro Phe 135	gta gag atg t Val Glu Met I	ac agt gaa atc 6 Yyr Ser Glu Ile 140	15
			Arg Glu Leu V	tc att ccc tgc 6 Val Ile Pro Cys .55	63
				ag ttt cca ctt 7 Lys Phe Pro Leu	11
				ac agt aga aag 7 Asp Ser Arg Lys 190	59
				ggg ctt ctg acc 8 ly Leu Leu Thr 205	07
				ac tat ctc aca 8 sn Tyr Leu Thr 220	55

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								agc Ser 285	1047
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	Asp							atc Ile				1671
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								aat Asn				1815
								gtg Val 555				1863
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								gtt Val				1959
								agt Ser				2007
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895 900 905 910

aac ttc aga aat gaa atc caa agc ttg gtc tag agtgaaaaac aacaaattca 2972 Asn Phe Arg Asn Glu Ile Gln Ser Leu Val 915 920

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3009

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<213> Artificial Sequence

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<223> Description of Artificial Sequence: Chimeric protein containing the extracellular domain of Flt-1 fused in-frame to the transmembrane and cytoplasmic domains of Fas

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Cys Leu Leu Thr Gly Ser Ser Gly Ser Lys Leu Lys Asp Pro 20 25 30

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Leu His Leu Gln Cys Arg Gly Glu Ala Ala His Lys Trp Ser Leu Pro 50 55 60

Glu Met Val Ser Lys Glu Ser Glu Arg Leu Ser Ile Thr Lys Ser Ala 65 70 75 80

Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser Thr Leu Thr Leu Asn Thr 85 90 95

Ala Gln Ala Asn His Thr Gly Phe Tyr Ser Cys Lys Tyr Leu Ala Val 100 105 110

Pro Thr Ser Lys Lys Glu Thr Glu Ser Ala Ile Tyr Ile Phe Ile 115 120 125

Ser Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu 130 135 140

Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val 145 150 155 160

Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr 165 170 175

Leu Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe 180 185 190

Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu 195 200 205

Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg 210 215 220

Gln Thr Asn Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val 225 230 235 240

Lys Leu Leu Arg Gly His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr 245 250 255

Pro Leu Asn Thr Arg Val Gln Met Thr Trp Ser Tyr Pro Asp Glu Lys 260 265 270

Asn Lys Arg Ala Ser Val Arg Arg Ile Asp Gln Ser Asn Ser His 280 275 Ala Asn Ile Phe Tyr Ser Val Leu Thr Ile Asp Lys Met Gln Asn Lys 295 Asp Lys Gly Leu Tyr Thr Cys Arg Val Arg Ser Gly Pro Ser Phe Lys 310 315 Ser Val Asn Thr Ser Val His Ile Tyr Asp Lys Ala Phe Ile Thr Val 325 330 Lys His Arg Lys Gln Gln Val Leu Glu Thr Val Ala Gly Lys Arg Ser 345 Tyr Arg Leu Ser Met Lys Val Lys Ala Phe Pro Ser Pro Glu Val Val 360 Trp Leu Lys Asp Gly Leu Pro Ala Thr Glu Lys Ser Ala Arg Tyr Leu 375 Thr Arg Gly Tyr Ser Leu Ile Ile Lys Asp Val Thr Glu Glu Asp Ala 390 395 Gly Asn Tyr Thr Ile Leu Leu Ser Ile Lys Gln Ser Asn Val Phe Lys 405 410 Asn Leu Thr Ala Thr Leu Ile Val Asn Val Lys Pro Gln Ile Tyr Glu 425 420 Lys Ala Val Ser Ser Phe Pro Asp Pro Ala Leu Tyr Pro Leu Gly Ser 440 Arg Gln Ile Leu Thr Cys Thr Ala Tyr Gly Ile Pro Gln Pro Thr Ile 455 460 Lys Trp Phe Trp His Pro Cys Asn His Asn His Ser Glu Ala Arg Cys 470 475 Asp Phe Cys Ser Asn Asn Glu Glu Ser Phe Ile Leu Asp Ala Asp Ser 490 Asn Met Gly Asn Arg Ile Glu Ser Ile Thr Gln Arg Met Ala Ile Ile 505 Glu Gly Lys Asn Lys Met Ala Ser Thr Leu Val Val Ala Asp Ser Arg 520 Ile Ser Gly Ile Tyr Ile Cys Ile Ala Ser Asn Lys Val Gly Thr Val 535 540 Gly Arg Asn Ile Ser Phe Tyr Ile Thr Asp Val Pro Asn Gly Phe His 555 550 Val Asn Leu Glu Lys Met Pro Thr Glu Gly Glu Asp Leu Lys Leu Ser 570 Cys Thr Val Asn Lys Phe Leu Tyr Arg Asp Val Thr Trp Ile Leu Leu 585 Arg Thr Val Asn Asn Arg Thr Met His Tyr Ser Ile Ser Lys Gln Lys 600 Met Ala Ile Thr Lys Glu His Ser Ile Thr Leu Asn Leu Thr Ile Met Asn Val Ser Leu Gln Asp Ser Gly Thr Tyr Ala Cys Arg Ala Arg Asn 630 635 Val Tyr Thr Gly Glu Glu Ile Leu Gln Lys Lys Glu Ile Thr Ile Arg 650 Asp Gln Glu Ala Pro Tyr Leu Leu Arg Asn Leu Ser Asp His Thr Val 665 Ala Ile Ser Ser Ser Thr Thr Leu Asp Cys His Ala Asn Gly Val Pro 680 Glu Pro Gln Ile Thr Trp Phe Lys Asn Asn His Lys Ile Gln Glu 700 695 Pro Gly Ile Ile Leu Gly Pro Gly Ser Ser Thr Leu Phe Ile Glu Arg 715

Val Thr Glu Glu Asp Glu Gly Val Tyr His Cys Lys Ala Thr Asn Gln 730 725 Lys Gly Ser Val Glu Ser Ser Ala Tyr Leu Thr Val Gln Gly Thr Ser 740 745 Asp Gly Ser Arg Ser Asn Leu Gly Trp Leu Cys Leu Leu Leu Pro 760 Ile Pro Leu Ile Val Trp Val Lys Arg Lys Glu Val Gln Lys Thr Cys 780 775 Arg Lys His Arg Lys Glu Asn Gln Gly Ser His Glu Ser Pro Thr Leu 795 790 Asn Pro Glu Thr Val Ala Ile Asn Leu Ser Asp Val Asp Leu Ser Lys 805 810 Tyr Ile Thr Thr Ile Ala Gly Val Met Thr Leu Ser Gln Val Lys Gly 820 825 Phe Val Arg Lys Asn Gly Val Asn Glu Ala Lys Ile Asp Glu Ile Lys 840 835 Asn Asp Asn Val Gln Asp Thr Ala Glu Gln Lys Val Gln Leu Leu Arg 855 860 Asn Trp His Gln Leu His Gly Lys Lys Glu Ala Tyr Asp Thr Leu Ile 870 875 Lys Asp Leu Lys Lys Ala Asn Leu Cys Thr Leu Ala Gly Lys Ile Gln 885 890 Thr Ile Ile Leu Lys Asp Ile Thr Ser Asp Ser Glu Asn Ser Asn Phe 905 900 Arg Asn Glu Ile Gln Ser Leu Val 915 920

<210> 9

<211> 3009

<212> DNA

<213> Artificial Sequence

<220>

<221> CDS

<222> (169)..(2952)

<220>

<223> Description of Artificial Sequence: Nucleic acid construct encoding chimeric protein containing the extracellular domain of Flk-1 fused in-frame to the transmembrane and cytoplasmic domains of Fas

<400> 9
gegggtaeeg cegeeggteg gegeeegge teectageee tgtgegetea actgteetge 60
getgegggt geegegagtt ceaceteege geeteettet etagaeagge getgggagaa 120
agaaeegget eeegagttet gggeattteg eeeggetega ggtgeagg atg eag age 177

Met Gln Ser 1

aag gtg ctg ctg gcc gtc gcc ctg tgg ctc tgc gtg gag acc cgg gcc 225
Lys Val Leu Leu Ala Val Ala Leu Trp Leu Cys Val Glu Thr Arg Ala
5 10 15

tct Ser								273
caa Gln								321
tgc Cys								369
ggc Gly								417
tgt Cys 85								465
tac Tyr								513
tat Tyr								561
cat His								609
cca Pro								657
tac Tyr 165								705
agc Ser								753
atg Met								801
atg Met								849
agt Ser								897

		Cys	aca Thr													945
	Glu		cct Pro													993
			acc Thr													1041
			gat Asp 295													1089
			agt Ser													1137
gtc Val	cat His 325	gaa Glu	aaa Lys	cct Pro	ttt Phe	gtt Val 330	gct Ala	ttt Phe	gga Gly	agt Ser	ggc Gly 335	atg Met	gaa Glu	tct Ser	ctg Leu	1185
			acg Thr													1233
			ccc Pro													1281
			cac His 375													1329
			aga Arg													1377
			gag Glu													1425
cca Pro 420	ccc Pro	cag Gln	att Ile	ggt Gly	gag Glu 425	aaa Lys	tct Ser	cta Leu	Ile	tct Ser 430	cct Pro	gtg Val	gat Asp	tcc Ser	tac Tyr 435	1473
cag Gln	tac Tyr	ggc Gly	acc Thr	act Thr 440	caa Gln	acg Thr	ctg Leu	Thr	tgt Cys 445	acg Thr	gtc Val	tat Tyr	Ala	att Ile 450	cct Pro	1521
			cac His 455				Tyr									1569

											cca Pro					1617
											aat Asn 495					1665
											aac Asn					1713
											ttg Leu					1761
											atc Ile					1809
											atg Met					1857
											aga Arg 575					1905
aac Asn 580	ctc Leu	aca Thr	tgg Trp	tac Tyr	aag Lys 585	ctt Leu	ggc Gly	cca Pro	cag Gln	cct Pro 590	ctg Leu	cca Pro	atc Ile	cat His	gtg Val 595	1953
											gat Asp					2001
											gac Asp					2049
											gac Asp					2097
gct Ala	caa Gln 645	gac Asp	agg Arg	aag Lys	acc Thr	aag Lys 650	aaa Lys	aga Arg	cat His	tgc Cys	gtg Val 655	gtc Val	agg Arg	cag Gln	ctc Leu	2145
											gga Gly					2193
cag Gln	acg Thr	aca Thr	agt Ser	att Ile 680	gly ggg	gaa Glu	agc Ser	atc Ile	gaa Glu 685	gtc Val	tca Ser	tgc Cys	acg Thr	gca Ala 690	tct Ser	2241

				cag Gln								2289
				att Ile								2337
				aag Lys								2385
				tgt Cys 745								2433
				gga Gly								2481
				cca Pro							_	2529
_				aag Lys								2577
				cct Pro								2625
				atc Ile 825								2673
	_			gtt Val	_	_		_	-	_		2721
				gac Asp								2769
				tgg Trp								2817
-		-		gat Asp								2865
				atc Ile 905								2913

aat tca aac ttc aga aat gaa atc caa agc ttg gtc tag agtgaaaaac 2962 Asn Ser Asn Phe Arg Asn Glu Ile Gln Ser Leu Val 920 925

aacaaattca gttctgagta tatgcaatta gtgtttgaaa agattct

3009

<210> 10

<211> 927

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Chimeric protein containing the extracellular domain of Flk-1 fused in-frame to the transmembrane and cytoplasmic domains of Fas

<400> 10 Met Gln Ser Lys Val Leu Leu Ala Val Ala Leu Trp Leu Cys Val Glu 10 Thr Arg Ala Ala Ser Val Gly Leu Pro Ser Val Ser Leu Asp Leu Pro 25 Arg Leu Ser Ile Gln Lys Asp Ile Leu Thr Ile Lys Ala Asn Thr Thr 40 Leu Gln Ile Thr Cys Arg Gly Gln Arg Asp Leu Asp Trp Leu Trp Pro 55 Asn Asn Gln Ser Gly Ser Glu Gln Arg Val Glu Val Thr Glu Cys Ser 70 75 Asp Gly Leu Phe Cys Lys Thr Leu Thr Ile Pro Lys Val Ile Gly Asn 90 Asp Thr Gly Ala Tyr Lys Cys Phe Tyr Arg Glu Thr Asp Leu Ala Ser 105 Val Ile Tyr Val Tyr Val Gln Asp Tyr Arg Ser Pro Phe Ile Ala Ser 120 125 Val Ser Asp Gln His Gly Val Val Tyr Ile Thr Glu Asn Lys Asn Lys 135 Thr Val Val Ile Pro Cys Leu Gly Ser Ile Ser Asn Leu Asn Val Ser 150 155 Leu Cys Ala Arg Tyr Pro Glu Lys Arg Phe Val Pro Asp Gly Asn Arg 165 170 Ile Ser Trp Asp Ser Lys Lys Gly Phe Thr Ile Pro Ser Tyr Met Ile 185 190 Ser Tyr Ala Gly Met Val Phe Cys Glu Ala Lys Ile Asn Asp Glu Ser 200 Tyr Gln Ser Ile Met Tyr Ile Val Val Val Gly Tyr Arg Ile Tyr 215 220 Asp Val Val Leu Ser Pro Ser His Gly Ile Glu Leu Ser Val Gly Glu 230 235 Lys Leu Val Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn Val Gly Ile 250 Asp Phe Asn Trp Glu Tyr Pro Ser Ser Lys His Gln His Lys Lys Leu 265 Val Asn Arg Asp Leu Lys Thr Gln Ser Gly Ser Glu Met Lys Lys Phe 275 280

Leu Ser Thr Leu Thr Ile Asp Gly Val Thr Arg Ser Asp Gln Gly Leu Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met Thr Lys Lys Asn Ser Thr Phe Val Arg Val His Glu Lys Pro Phe Val Ala Phe Gly Ser Gly Met Glu Ser Leu Val Glu Ala Thr Val Gly Glu Arg Val Arg Ile Pro Ala Lys Tyr Leu Gly Tyr Pro Pro Pro Glu Ile Lys Trp Tyr Lys Asn Gly Ile Pro Leu Glu Ser Asn His Thr Ile Lys Ala Gly His Val Leu Thr Ile Met Glu Val Ser Glu Arg Asp Thr Gly Asn Tyr Thr Val Ile Leu Thr Asn Pro Ile Ser Lys Glu Lys Gln Ser His Val Val Ser Leu Val Val Tyr Val Pro Pro Gln Ile Gly Glu Lys Ser Leu Ile Ser Pro Val Asp Ser Tyr Gln Tyr Gly Thr Thr Gln Thr Leu Thr Cys Thr Val Tyr Ala Ile Pro Pro Pro His His Ile His Trp Tyr Trp Gln Leu Glu Glu Glu Cys Ala Asn Glu Pro Ser Gln Ala Val Ser Val Thr Asn Pro Tyr Pro Cys Glu Glu Trp Arg Ser Val Glu Asp Phe Gln Gly Gly Asn Lys Ile Glu Val Asn Lys Asn Gln Phe Ala Leu Ile Glu Gly Lys Asn Lys Thr Val Ser Thr Leu Val Ile Gln Ala Ala Asn Val Ser Ala Leu Tyr Lys Cys Glu Ala Val Asn Lys Val Gly Arg Gly Glu Arg Val Ile Ser Phe His Val Thr Arg Gly Pro Glu Ile Thr Leu Gln Pro Asp Met Gln Pro Thr Glu Glu Ser Val Ser Leu Trp Cys Thr Ala Asp Arg Ser Thr Phe Glu Asn Leu Thr Trp Tyr Lys Leu Gly Pro Gln Pro Leu Pro Ile His Val Gly Glu Leu Pro Thr Pro Val Cys Lys Asn Leu Asp Thr Leu Trp Lys Leu Asn Ala Thr Met Phe Ser Asn Ser Thr Asn Asp Ile Leu Ile Met Glu Leu Lys Asn Ala Ser Leu Gln Asp Gln Gly Asp Tyr Val Cys Leu Ala Gln Asp Arg Lys Thr Lys Lys Arg His Cys Val Val Arg Gln Leu Thr Val Leu Glu Arg Val Ala Pro Thr Ile Thr Gly Asn Leu Glu Asn Gln Thr Thr Ser Ile Gly Glu Ser Ile Glu Val Ser Cys Thr Ala Ser Gly Asn Pro Pro Pro Gln Ile Met Trp Phe Lys Asp Asn Glu Thr Leu Val Glu Asp Ser Gly Ile Val Leu Lys Asp Gly Asn Arg Asn Leu Thr Ile Arg Arg Val Arg Lys Glu Asp Glu Gly Leu Tyr Thr

Cys Gln Ala Cys Ser Val Leu Gly Cys Ala Lys Val Glu Ala Phe Phe 745 740 Ile Ile Glu Gly Ala Gln Glu Lys Gly Ser Arg Ser Asn Leu Gly Trp 760 Leu Cys Leu Leu Leu Pro Ile Pro Leu Ile Val Trp Val Lys Arg 775 780 770 Lys Glu Val Gln Lys Thr Cys Arg Lys His Arg Lys Glu Asn Gln Gly 790 795 Ser His Glu Ser Pro Thr Leu Asn Pro Glu Thr Val Ala Ile Asn Leu 805 810 Ser Asp Val Asp Leu Ser Lys Tyr Ile Thr Thr Ile Ala Gly Val Met 825 830 Thr Leu Ser Gln Val Lys Gly Phe Val Arg Lys Asn Gly Val Asn Glu 840 Ala Lys Ile Asp Glu Ile Lys Asn Asp Asn Val Gln Asp Thr Ala Glu 860 855 Gln Lys Val Gln Leu Leu Arg Asn Trp His Gln Leu His Gly Lys Lys 870 875 Glu Ala Tyr Asp Thr Leu Ile Lys Asp Leu Lys Lys Ala Asn Leu Cys 890 885 Thr Leu Ala Gly Lys Ile Gln Thr Ile Ile Leu Lys Asp Ile Thr Ser 905 900 Asp Ser Glu Asn Ser Asn Phe Arg Asn Glu Ile Gln Ser Leu Val 920 925 915 <210> 11 <211> 27 <212> DNA <213> Artificial Sequence <223> Description of Artificial Sequence: Primer <400> 11 27 gcggaattca ggggcgggca ctggcac <210> 12 <211> 30 <212> DNA <213> Artificial Sequence <223> Description of Artificial Sequence: Primer <400> 12 30 ggctcgagaa tcttttcaaa cactaattgc

<210> 13 <211> 30 <212> DNA

<213> Artificial Sequence

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<210> 14 <211> 28	
<212> DNA	
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<223> Description of Artificial Sequence: Primer	
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gcccggggtg aagaaagg aagtacag	28
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<223> Description of Artificial Sequence: Primer	
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gcgggtaccg cggccagcgg gcctggcgcc	30
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<400> 16	
ggcggatccg tccgaggttc cttgaacagt gagg	34
<210> 17	
<211> 30	
<212> DNA	
<213> Artificial Sequence	
<220>	
<223> Description of Artificial Sequence: Primer	
<400> 17	
gegggtaceg cegeeggteg gegeeeggge	30

<400> 22 gatggagttg aaggtagttt cgtg



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